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世界知的所有権機関

国際事務局

特許協力条約に基づいて公開された国際出願



(51) 国際特許分類6 C12N 15/11, C12Q 1/68 // G01N 33/566	A1	(11) 国際公開番号 WO 95/14772 (43) 国際公開日 1995年6月1日 (01.06.95)
(21) 国際出願番号 PCT/JP94/01916 (22) 国際出願日 1994年11月11日(11.11.94) (30) 優先権データ 特願平5/355504 1993年11月12日(12.11.93) JP (71) 出願人：および (72) 発明者 松原謙一(MATSUBARA, Kenichi)[JP/JP] 〒565 大阪府吹田市山田東3-18-1-804 Osaka, (JP) 大久保公策(OKUBO, Kousaku)[JP/JP] 〒562 大阪府箕面市瀬川2-11-26 Osaka, (JP) (74) 代理人 弁理士 吉田研二, 外(YOSHIDA, Kenji et al.) 〒180 東京都武蔵野市吉祥寺本町1丁目34番12号 Tokyo, (JP)	(81) 指定国 AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN, 欧州特許(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許(BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO特許(KE, MW, SD, SZ). 添付公開書類 国際調査報告書 補正書	
(54) Title : GENE SIGNATURE (54) 発明の名称 ジーン・シグナチャー (57) Abstract A 3'-directed cDNA library which accurately reflects the abundance ratio of mRNA in a cell has been prepared from various human tissues, and sequencing of the cDNAs contained in the library has been conducted to examine the incidence of each cDNA in each tissue. As each cDNA has expression information with each tissue corresponding to the mRNA concentration, these cDNAs are usable as a probe or primer for detecting cell anomaly or discriminating cells. The cloned gene can produce proteins utilizable as a medicine or the like.		

Identifier: AAN00001 DNA Sequence 134 BP

Release Info: Derwent Geneseq Database Release No. 200124; Date released 26-NOV-01

Database
XReference: WPI; 1995-206931/27.

Accession
Number: AAT22548

Patent Title: Identifying gene signatures in 3'-directed human cDNA library - e.g. for diagnosis of abnormal cell function, by preparing cDNA that reflects relative abundance of corresp. mRNA in specific human tissues

Patented by: (MATS/) MATSUBARA K.;(OKUB/) OKUBO K.

Inventor: Matsubara K, Okubo K

Description: Human gene signature HUMGS04161.

Patent
Number: WO9514772-A1

Patent
Publication Date: 01-JUN-1995

Modification
Date: 01-OCT-1996 (first entry)

Local Filing: 11-NOV-1994; 94WO-JP01916

Priority: 12-NOV-1993

Abstract: A single-stranded DNA (or its complementary strand or the corresp. double-stranded DNA) which comprises one of the 7837 "GS" sequences given in AAT19001-T26837 and which is able to hybridise to part of human genomic DNA, cDNA or mRNA is claimed. The GS (Gene Signature) sequences were obtained from 3'-directed cDNA libraries prepared from various human tissues; synthesis of cDNA was initiated from the 3'-end of mRNA by using poly(T) as the sole primer. Since the 3'- untranslated sequence is unique to a particular mRNA species, almost all the 3'-oriented cDNAs hybridise with specific mRNAs. Each library is constructed so as to reflect accurately the relative abundance of different mRNAs in the particular tissue from which it was derived. The appearance frequency of a given GS in a cDNA library can be determined (esp. using primers and probes derived from the GS sequences) as a means of diagnosing abnormal cell function or for recognising different cell types.

KeyWords: Gene signature;messenger RNA;mRNA;relative abundance;frequency;human;cloning;mapping;non-biased library;diagnosis;detection;cell typing;abnormal cell function;ss.

Organism: Homo sapiens.

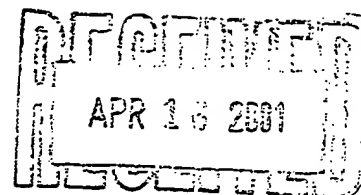
Sequence
Composition: Sequence 134 BP; 32 A; 31 C; 47 G; 23 T; 1 other;

Sequence: >AAT22548 WO9514772-A1 PA (MATS/) MATSUBARA PR 12-NOV-1993 PF 11-NOV-1994 Human gene signature HUMGS04161. [Homo sapiens.]
GATCTGGACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTANAGGA
CCCCGAGAGGGTGCACTGGAGCCCTGAGCATTGTAATATGCGGCCAGCCTATAAACAG
CTCCCGTGCTTAAA

DEX-0115

AF

PATENT COOPERATION TREATY



From the INTERNATIONAL SEARCHING AUTHORITY

To:
JANE MASSEY LICATA
LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

Docket System ☒
Status Report ☒
Docket Book ☒
6/12/01 ans

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing
(day/month/year)

12 APR 2001

Applicant's or agent's file reference
DEX-0114

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US00/31896

International filing date
(day/month/year)

21 November 2000 (21.11.2000)

Applicant
DLADEXUS, INC.

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.
Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.
If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer
Steph LeRawlings
Stephen LeRawlings, Ph.D.
Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
JANE MASSEY LICATA
LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing (day/month/year)	12 APR 2001
Applicant's or agent's file reference DEX-0114	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US00/31896	International filing date (day/month/year) 21 November 2000 (21.11.2000)
Applicant DIADEXUS, INC.	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.
Filing of amendments and statement under Article 19:
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

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3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices;

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

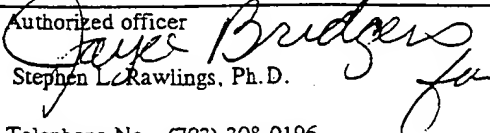
4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.
 If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231
 Facsimile No. (703) 305-3230

Authorized officer

 Stephen L. Rawlings, Ph.D.
 Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DEX-0114	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/31896	International filing date (day/month/year) 21 November 2000 (21.11.2000)	(Earliest) Priority Date (day/month/year) 22 November 1999 (22.11.1999)
Applicant DIADEXUS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☒ Unity of invention is lacking (See Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-7 and 16

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/00, 48/00, 49/00; C07H 21/02, 21/04; C07K 14/00; C12N 15/11, 15/63; C12P 19/34; C12Q 1/68; G01N 33/53

US CL : 424/9.1, 9.21, 84.1, 277.1; 435/6, 7.1, 91.2, 320.1; 514/44; 530/350; 536/23.1, 23.5, 24.31, 24.33

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/9.1, 9.21, 84.1, 277.1; 435/6, 7.1, 91.2, 320.1; 514/44; 530/350; 536/23.1, 23.5, 24.31, 24.33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	Database GenCore on GenEmbl, Accession No. AK000265, WATANABE, K, et al. 'Homo sapiens cDNA FLJ20258 fis, clone COLF7250'. 15 February 2000.	1, 2, 16
A,P	Database GenCore on GenEmbl, Accession No. AF282167, WU, K, et al. 'Cloning and expression analyses of down-regulated cDNA C6-2A in human esophageal cancer'. Homo sapiens DR3 mRNA, complete sequence, 26 June 2000.	1, 2, 16
A,P	Database CANCERLIT on STN, AN 2000409461, BODEY, B, et al. 'Failure of cancer vaccines: the significant limitations of this approach to immunotherapy'. Anticancer Research. 2000, Vol. 20, pages. 2665-2676 (abstract only).	16
A	Database CA on STN, AN 1998-0161021, GOODISON, S. et al. 'Current status of CD44 variant isoforms as cancer diagnostic markers'. Histopathology. 1998, Vol. 32, pp. 1-6 (bibliography only)	1-7

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.*** Special categories of cited documents:**

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

08 March 2001 (08.03.2001)

Date of mailing of the international search report

Authorized officer

Stephen L. Rawlings, Ph.D.

Telephone No. (703) 308-0196

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks

Box PCT

Washington, D.C. 20231

Facsimile No. (703)305-3230

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/31896

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7 and 16, drawn to a diagnostic marker comprising SEQ ID NO: 1, a method of using said diagnostic marker to diagnose, monitor, and/or stage cancer in a patient, and a vaccine comprising said marker.

Group II, claim(s) 8, drawn to a method of identifying potential therapeutic agents.

Group III, claim(s) 9, drawn to an antibody.

Group IV, claim(s) 10 and 11, drawn to a method of imaging cancer in a patient.

Group V, claim(s) 12 and 13, drawn to a method of treating cancer in a patient comprising administering an antibody that specifically binds Ovr107.

Group VI, claim(s) 14, in so far as the claim is drawn to a method of treating cancer in a patient comprising administering a molecule that downregulates expression of Ovr107.

Group VII, claim(s) 14, in so far as the claim is drawn to a method of treating cancer in a patient comprising administering a molecule that downregulates activity of Ovr107.

Group VIII, claim(s) 15, drawn to a method of inducing an immune response in a patient.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions are distinct, each from the other because of the following reasons:

Group I does not share a common technical feature with Groups II-VIII and PCT Rules 13.1 and 13.2 do not provide for multiple products and methods.

Continuation of B. FIELDS SEARCHED Item 3: All commercial sequence data bases (GenEmbl, Geneseq, Issued Patents, Est), Cancerlit, Medline, STN: medicine cluster

Search terms: SEQ ID NO: 1, Ovr107, ovarian cancer, gynecologic cancer, malignancy, tumor, diagnosis, treatment; immunization; vaccine; gene therapy, staging, Gene no. 403869, Clone no. 817834, DIADEXUS, INC.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be couched with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

L8 ANSWER 3 OF 3 PASCAL COPYRIGHT 2001 INIST-CNRS. ALL RIGHTS RESERVED.
AN 1998-0161021 PASCAL
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TIEN Current status of CD44 variant isoforms as cancer
diagnostic markers
AU GOODISON S.; TARIN D.
CS Nuffield Department of Pathology and Bacteriology University of Oxford,
John Radcliffe Hospital, Oxford, United Kingdom
SO Histopathology, (1998), 32(1), 1-6, 37 refs.
ISSN: 0309-0167
DT Journal
BL Analytic
CY United Kingdom
LA English
AV INIST-17811, 354000078763200010
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.

L23 ANSWER 1 OF 97 CANCERLIT
 AN 2000409461 CANCERLIT
 DN 20409461
 TI Failure of cancer vaccines: the significant limitations of this approach to immunotherapy.
 AU Bodey B; Bodey B Jr; Siegel S E; Kaiser H E
 CS Department of Pathology, University of Southern California, Los Angeles 91335, USA. Bodeyl8@aol.com
 SO ANTICANCER RESEARCH, (2000). Vol. 20, No. 4, pp. 2665-76.
 Journal code: 59L. ISSN: 0250-7005.
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 FS MEDL; L; Priority Journals; Cancer Journals
 LA English
 OS MEDLINE 20409461
 EM 200010
 AB Immunotherapy has always represented a very attractive fourth-modality therapeutic approach, especially in light of the many shortcomings of conventional surgery, radiation, and chemotherapies in the

management of cancer. Subsets of neoplastically transformed cells have been shown to (re-)express on their surface molecules which are not typically present on the surface of neighboring normal cells. In some instances, especially in malignant melanomas, cytotoxic T lymphocytes (CTLs) directed against such tumor associated antigens (TAAs) have been isolated. The cancer vaccine approach to therapy is based on the notion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate. However, due to the low immunogenicity of TAAs, downregulation of MHC molecules, the lack of adequate costimulatory molecule expression, secretion of immunoinhibitory cytokines, etc., such expectations are rarely fulfilled. Various approaches have been explored ranging from the use of irradiation inactivated whole-cell vaccines derived from both autologous and allogeneic tumors (even tumor cell lines), and genetically modified versions of such cellular vaccines which aim at correcting costimulatory dysfunction or altering the in situ humoral milieu to aid immune recognition and activation. Anti-idiotypic vaccines, based on cancer cell associated idiotypes, have also been explored which aim at increasing immunogenicity through in vivo generation of vigorous immune responses. Dendritic cell (DC) vaccines seek to improve the presentation of TAAs to naive T lymphocytes. Unfortunately, there is always the possibility of faulty antigen presentation which could result in tolerance induction to the antigens contained within the vaccine, and subsequent rapid tumor progression. The theoretical basis for all of these approaches is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained within the cancer vaccine has been documented

in

most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs in the context of the particular human

leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use. The use of cancer vaccines seems, at present, destined to remain limited to their employment as adjuvants to both traditional therapies and in the management of minimal residual disease following surgical resection of the primary cancer mass.

GenCore version 4.5
Copyright (c) 1993 - 2000 CompuGen Ltd.

OH nucleic - nucleic search, using sw model

Run on: March 3, 2001, 14:28:31 ; Search time 2615.3 Seconds

(without alignments)

8569.596 Million cell updates/sec

Title: pct-us00-31896a-1

Perfect score: 1635

Sequence: 1 tcggggccgagagccggc.....agatgggtgccanttnaaa 1635

Scoring table: IDENTITY_NUC

Gapop 10.0 , Gapext 1.0

Searched: 1118133-seqs, 6853842396 residues

Total number of hits satisfying chosen parameters: 2236266

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

GenEmbl :

1: gb_ba1.*

2: gb_ba2.*

3: gb_em.*

4: gb_ov.*

5: gb_ph.*

6: gb_pl1.*

7: gb_pl2.*

8: gb_pr1.*

9: gb_pr2.*

10: gb_pr3.*

11: gb_ro.*

12: gb_sy.*

13: gb_un.*

14: em_fun.*

15: em_hum1.*

16: em_hum2.*

17: em_in.*

18: em_em.*

19: em_or.*

20: em_ov.*

21: em_pat.*

22: em_ph.*

23: em_pl.*

24: em_ro.*

25: em_sy.*

26: em_un.*

27: em_v1.*

28: em_v2.*

29: gb_htg1.*

30: gb_htg2.*

31: gb_inl.*

32: gb_in2.*

33: em_ba1.*

34: em_ba2.*

35: em_hum3.*

36: em_hum4.*

37: gb_pr4.*

38: gb_htg3.*

39: gb_htg4.*

40: gb_htg5.*

41: gb_htg6.*

42: gb_htg7.*

43: em_htg1.*

44: em_htg2.*
45: em_htg3.*
46: em_hum5.*
47: gb_pl3.*
48: gb_pr5.*
49: gb_htg8.*
50: gb_htg9.*
51: gb_htg10.*
52: gb_htg11.*
53: gb_htg12.*
54: gb_htg13.*
55: gb_htg14.*
56: gb_in3.*
57: gb_htg15.*
58: gb_htg16.*
59: gb_htg17.*
60: em_htg4.*
61: em_htg5.*
62: em_htg6.*
63: em_htg7.*
64: em_hum6.*
65: gb_htg18.*
66: gb_htg19.*
67: gb_htg20.*
68: gb_htg21.*
69: gb_htg22.*
70: gb_htg23.*
71: gb_v11.*
72: gb_v12.*
73: gb_ba3.*
74: em_htg8.*
75: em_htg9.*
76: em_htg10.*
77: gb_pr6.*
78: gb_pr7.*
79: gb_sts1.*
80: gb_sts2.*
81: gb_pat1.*
82: gb_pat2.*
83: em_htg0.*
84: gb_htg24.*
85: gb_pr8.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB	ID	Description
1	1550	94.8	2228	37	AK000265	AK000265 Homo sapi
2	1403.4	85.8	1829	37	AF282167	AF282167 Homo sapi
3	419.6	25.7	35197	9	AC005782	AC005782 Homo sapi
c 4	414.8	25.4	204340	42	AC019238	AC019238 Homo sapi
5	405.6	24.8	5985	37	AF282168	AF282168 Homo sapi
6	214.2	13.1	3102	37	AK025588	AK025588 Homo sapi
7	212.8	13.0	3074	37	AK025824	AK025824 Homo sapi
8	151	9.2	188302	38	AC011476	AC011476 Homo sapi
c 9	132.4	8.1	142203	65	AC079521	AC079521 Mus muscu
10	92.2	5.6	1245	81	157340	157340 Sequence 3
11	92.2	5.6	1245	11	MUS858A	L21671 Mouse Esp8
12	89.2	5.5	3110	32	AF208262	AF208262 Drosophill
c 13	89.2	5.5	90816	41	AC017493	AC017493 Drosophill
14	89.2	5.5	102389	31	AC004546	AC004546 Drosophill
c 15	89.2	5.5	299378	31	AE003588	AE003588 Drosophill
16	84.8	5.2	2148	37	AK025175	AK025175 Homo sapi
17	74.4	4.6	3832	78	HSU12535	U12535 Human epide
c 18	61.0	3.8	180144	51	AC023429	AC023429 Homo sapi
19	57.4	3.5	81767	49	AC021929	AC021929 Homo sapi
c 20	56	3.4	78220	50	AC023212	AC023212 Homo sapi
c 21	56	3.4	158523	39	AC013547	AC013547 Homo sapi

